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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,618	12/17/2001	Guido Henning	Le A 35 010	1214

7590 09/07/2007

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/022,618	HENNING ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,3-5 and 12-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 3-5, 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed June 14, 2007 in response to the Office Action of December 14, 2007 is acknowledged and has been entered. Previously pending claims 1, 15 have been amended and new claims 16 and 17 have been added. Claims 1, 3-5, 12-17 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 3, 5, 12, 15 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed December 14, 2006, Section 5, pages 2-7.

Applicant argues that the markers of Pillai et al fall in the category of markers that are present both in healthy cells and tumor cells and thus detection of these particular markers mentioned by Pillai would not have been expected by persons skilled in the art to be reliable indicators of the presence of tumor cells or their precursor cells in a uterine cervical smear. The argument has been considered but has not been found persuasive because although the markers disclosed in Pillai

et al are cancer cell markers that are not exclusively found in cervical cancer cells, the claims as currently constituted are not drawn specifically to any particular cancer type and require only that cancer cells by detected in uterine cervical smears. Further, given the teaching in Pillai et al that these markers are cancer markers, that these are found in cervical smears and cervical cancer cells, it is unclear why Applicant has questioned the reliability of these "particular" markers for determining tumor cells in cervical smears. Given these teachings one would certainly believe it more likely than not and expect that these known cancer markers, found to be associated with cervical cancer cells in cervical smears would reliably detect cancer cells within the smear. In addition, Applicant is arguing the Pillai reference individually without clearly addressing the combined teachings of the combined references. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In re Young, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In re Keller 642 F.2d 413,208 USPQ 871 (CCPA 1981). It is further noted that Pillai et al specifically teaches a method for detecting tumor cells comprising assay for the presence of multiple markers for cervical cancer and thus it would appear that one of ordinary skill in the art would have a reasonable expectation of successfully detecting tumor cells.

Applicant argues that Geiger's teachings are not clearly applicable to Pillai because the combined method would still not have the color signal intensities combining and accrediting as required by the instant claims. The argument has

been considered but has not been found persuasive because Applicant is again arguing references individually without clearly addressing the combined teachings of the combined references as Guilano et al is cited to specifically addresses the color intensity and accrediting limitations. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In re Young, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In re Keller 642 F.2d 413,208 USPQ 871 (CCPA 1981).

Applicant argues that Pillai and Geiger together would not reliably indicate the presence of tumor cells and their precursors in the uterine cervical smears. The argument has been considered but has not been found persuasive because for the reasons set forth above and further because Applicant is arguing the references individually.

Applicant argues that even if the rejected claims could be considered to be prima facie obvious over such a combination, this is rebutted by the results reported in the instant specification about the reliability of the instant method. The argument has been considered but has not been found persuasive because the specification does not disclose the term "reliability".

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 1, 4, 13 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed December 14, 2006, Section 6, pages 7-9.

Applicant reiterates the arguments set forth above and further argues that Kihana and Giuliano do not bridge the gap between the instant claims and the combination of Pillai and Geiger. The argument has been considered but has not been found persuasive as drawn to the combination of Pillai and Geiger for the reasons set forth above. Further, it is noted that Applicant presents no arguments as to why Pillai and Geiger in combination with Giuliano does not make obvious the claimed invention other than to state that the gap is not bridged. The combination of Pillai, Geiger and Giuliano make obvious the claimed invention for the reasons previously set forth and none of the arguments set forth in the instant response have been found persuasive to overcome the rejection under 35 USC 103 previously set forth.

Further, as drawn to Kihana, no arguments, other than the statement that this reference does not bridge the gap are set forth. This argument is not found persuasive.

Applicant's arguments have not been found persuasive and the rejection is maintained.

7. Claim 14 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed December 14, 2006, Section 7, pages 9-10.

Because applicant did not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains,

> or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 16-17 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "wherein the detection of each of the markers alone is not a reliable indicator of the presence of tumor cells or their precursors" has no clear support in the specification and the claims as originally filed. A review of the specification and claims as originally filed revealed no mention of the phrase "markers alone" or the phrase "reliable indicator". Applicant states at page 8 of the response that support for the newly added claim language is supported at paragraph 0015 of US 2002/0106685. A review of paragraph 0015 of US 2002/0106685 reveals that the paragraphs discloses that

> [0015] The invention relates to molecular markers which, on being detected individually, do not achieve sufficient specificity with regard to recognizing pathologically altered cells or tissues since they are also partly present, in similar or different quantities, in biological material which is not pathologically altered. This is based on the fact that these markers can be proteins which are involved in physiological regulation processes in healthy cells as well. In addition to this, because of the antibody crossreacting nonspecifically, the detection of the molecular marker may not be unambiguous, with this being manifested in the staining of particles of the biological material which do not contain the molecular marker. The inventors have made the observation that the deficient specificity associated with the detection of single markers can be offset, so as to ensure higher specificity when detecting abnormal cells or tissue sections, by simultaneously detecting at least two markers in a cell. Consequently, greater informative value in the diagnosis of biological samples is achieved by combining several markers in a cell than by using single markers.

The cited support has been considered but has not been found persuasive because although the paragraph states that the markers "do not achieve sufficient specificity", this is clearly not the same as the marker "is not a reliable indicator" since many of these markers are well known as markers for disease. Although the

claims as currently constitute are drawn to the absolute limitation that the marker alone is not reliable, this is clearly not what the specification is teaching. Neither the specification nor the art of record states or implies that the markers alone are not reliable to any degree and the art recognizes that reliability of any diagnostic test is based specifically on the sensitivity and specificity of the test being used wherein reliability is relative based on those parameters. The subject matter claimed in claims 16-17 broadens the scope of the invention as originally disclosed in the specification.

10. Claims 16-17 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of "wherein combined and accredited signal intensities above or below the threshold value reliably indicate the presence of tumor cells and/or their precursors in thereby detecting tumor cells and their precursor cells in the uterine cervical smear" has no clear support in the specification and the claims as originally filed. A review of the specification and claims as originally filed revealed no mention of the phrase "signal intensities above or below the threshold value.....detecting tumor cells....." or the phrase "reliable indicator". Applicant states at page 8 of the response that support for the newly added claim language is supported at paragraph 0017 of US 2002/0106685. A review of paragraph 0017 of US 2002/0106685 reveals that the paragraphs discloses that

> [0017] According to the invention, the applicants' findings are used for a method for the early diagnosis of disease-associated cells or tissue sections which comprises detecting combinations of the described molecular markers with the aim of using automation to detect carcinomas and their precursors. The automated and specific detection of tumour cells can be ensured by the following method: firstly, at least two signals must be present in a cell and, secondly, the signal for each of the two markers must in each case be greater than an individually defined intensity or an individually defined threshold value.

> By using these two criteria, it is possible to regard those cells which, for example, express a marker above the set threshold, or exhibit stainings for the two markers which are below the respectively defined signal strength, as being healthy.

The cited support has been considered but has not been found persuasive because although the paragraph states that "the signal for each of the two markers must in each case be greater than an individually defined intensity or an individually defined threshold value", this is clearly not the same the claimed "signal intensities above or below the threshold value.....detecting tumor cells" as currently claimed. Further there is no teaching in the cited support drawn to the reliability indicating the presence of tumor cells and/or their precursors as claimed. The subject matter claimed in claims 16-17 broadens the scope of the invention as originally disclosed in the specification.

11. No claims allowed.

12. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be

proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

13. A reply under 37 CFR 1.113 to a final rejection must include the appeal from, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

14. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
August 21, 2007